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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,819	04/14/2004	Suzanne M.J. Fleiszig	UOCB-0006	5639

23377 7590 05/31/2007

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EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
05/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,819	FLEISZIG ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-11,20,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *20* is/are allowed.

6)☐ Claim(s) *1,6-11 and 24* is/are rejected.

7)☒ Claim(s) *2 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

ACKNOWLEDGMENT OF AMENDMENT, REMARKS AND STATUS OF THE CLAIMS

1. The amendment and remarks filed 03/19/07 are acknowledged, entered and considered. In view of Applicant's request claims 1, 8 and 20 have been amended, claims 3-5, 12-19, 21 and 22 have been canceled and claims 23 and 24 have been added. Claims 1, 2, 6-11, 20, 23 and 24 are now pending in the application. The objection to the trademarks and the rejection under 35 U.S.C. 112, first paragraph for claims 3-5 and 20 are withdrawn in view of Applicant's cancellation of claims, amendment and remarks filed 03/19/07. However, the rejection under 35 U.S.C. 112, first paragraph for claims 1 and 6-11 are maintained for the reasons of record.

ARGUMENTS ARE NOT PERSUASIVE

CLAIMS REJECTION-35 U.S.C. 112 1st PARAGRAPH.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 6-11 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing an ophthalmic composition comprising a collectin such as

surfactant proteins in a kit and in antimicrobial lens formulation thereof, and a method for treating an ocular disease caused by a bacterial microbe in a subject, the method comprising administering into the eye of a subject, a pharmaceutical composition comprising a therapeutically effective amount of a surfactant protein, does not reasonably provide enablement for a method of treating an ocular disease caused by a bacterial microbe in a subject, the method comprising administering into the eye of a subject, a pharmaceutical composition comprising a therapeutically effective amount of a **collectin** in the manner claimed in claims 1 and 6-11. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with claims 1 and 6-11.

Applicant's arguments filed 03/19/07 have been fully considered but they are not persuasive. Applicant has argued that the full scope of the claims is enabled, however, solely to expedite prosecution, Applicant has amended the claims to recite that the ocular disease is one that is caused by a bacterial microbe. To the extent the rejection applies to the claims as amended, Applicant traverse and request reconsideration because there is no evidence of record suggesting that a skilled practitioner would be unable to carry out the claimed method is unpersuasive. It is noted that Applicant has amended independent claim 1 to a method for treating an ocular disease caused by a bacterial microbe in a subject, thereby limiting claim 1 and claims

dependent thereof to treating an ocular disease caused by a bacterial microbe instead of microbe in general. However, claim 1 as drafted is still directed broadly to a method for treating an ocular disease caused by a bacterial microbe in a subject, the method comprising administering into the eye of a subject, a pharmaceutical composition comprising a therapeutically effective amount of a **collectin**.

"**Collectins**" as defined on paragraph 0055 in the instant specification comprise a family of innate immune molecules characterized by the presence of a collagen-like domain and a calcium-dependent lectin domain, commonly referred to as a carbohydrate recognition domain. The known collectins include surfactant protein-A, surfactant protein-D, CL-43, serum mannan-binding protein (MBP) also referred as serum mannan-binding lectin (MBL), and conglutinin. On paragraph 0056 the instant specification states that the collectins can be divided into families based on their quaternary structure. Typically, collectins exist in oligomeric form comprising trimeric subunits. Each subunit consists of four major domains: a short cysteine-containing NH_2 terminal cross-linking domain; a triple helical collagen domain of variable length; a trimeric coiled-coil linking domain; and a carboxyl terminal, C-type lectin carbohydrate recognition domain. Further, on paragraph 0057 the specification states that collectins are expressed in various sites throughout the body. Although, originally identified as an essential part of both the physiological and immune defense functions of the airways, it has recently

became apparent that collectins are present at other sites in the human body and can form an important part of the mucosal immune defense.

Thus, in view of the above, the term "**collectin**" is very broad and encompasses all the situation/conditions cited above. However, the instant specification teaches the method for preparing an ophthalmic composition comprising a collectin such as surfactant protein, which is a tear surfactant protein, i.e., SP-D in a kit and in antimicrobial lens formulation thereof (See e.g., paragraphs 0010 and 0011). Example 1 teaches the preparation of inocula by using strains of *Pseudomonas aeruginosa*, Example 2 discloses the collections of tears from human subjects, Example 3 shows the culturing of rabbit corneal epithelial cells using anti-SP-D antibody, Examples 4 and 5 teach bacterial growth assays and bacterial invasion assays using SP-D, respectively, Examples 7 and 8 are directed to ELISA for quantification surfactant protein D (SP-D) in tears and adsorption of SP-D from human tear fluid with Mannan-Sepharose. Similarly, Figures 1-7 disclose various *in vitro* assays, which show quantifications of bacterial invasion such as *P. aeruginosa* in corneal epithelial cells using SP-D.

Thus, there is no evidence in the instant specification to employ or administer the pharmaceutical composition comprising a therapeutically effective amount of **collectins** useful for treatment of bacterial ocular diseases in a subject as claimed, except for the mere recitation of protocols on pages 19-29 in the instant specification disclosing methods of

administering a collectin in general and/or surfactant proteins to the eye to treat bacterial ocular diseases in as subject without presenting any data or evidence to substantiate the protocols. Hence, the only support for the claimed method of treatment using the pharmaceutical composition in the specification is Applicant's supposition of the invention as recited in the protocols.

Further, the term "**collectin**" as defined above includes the various conditions or situations listed on paragraphs 0055-0079 as well as those commercially available collectins listed in paragraph 0079 in the instant specification. Thus, when these situations or conditions are added, undue experimentation would be required to determine which of the diseases conditions or situations would be treated by using the various recited collectins in the instant specification in the manner claimed in claims 1 and 6-11. Furthermore, Applicant's claims are directed to a very large number of collectins, which encompasses all kinds of variations recited in the instant specification, and there is no objective factual evidence in the specification showing that treatment has occurred using the undefined collectins pharmaceutical composition claimed. Thus, one cannot employ or use or administer undefined collectins pharmaceutical compositions in all situations without appropriate testing.

Therefore, in view of the above, the scope of the instantly claimed invention are very broad and speculative in that there is no working example or data or evidence which shows that the claimed compounds (i.e. collectins in general) are useful as a pharmaceutical compositions to treat ocular diseases caused by a bacterial microbe as

claimed in claims 1 and 6-11. It would include those that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since a vast range of collectins are intended to be administered in all kinds of possible treatment of ocular diseases caused by a bacterial microbe are contemplated and are encompassed as well as wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which is not clearly disclosed. Hence, one of ordinary skill in the art would not be able to identify all the ocular disease treatments caused by a bacterial microbe with wide range of collectins intended to be effective for the claimed purpose as encompassed in the claims would be effective and under what conditions.

Further, the first paragraph of 35 U.S.C. 112 requires, *inter alia,* that a patent specification provide sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, *id.* at 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Where practice of the full scope of the claims would require experimentation; factors to be considered in determining whether a disclosure would require undue experimentation ..... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance

presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Therefore, applying the *Wands* factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely broad claims fro the reasons given above. Thus, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data, and the breadth of the claims, the claims are not commensurate in scope with the enabling disclosure. Accordingly, filing of evidence commensurate with the scope of the claims or amendment of the claims to what is supported by the enabling disclosure is suggested.

The followings are new grounds of objection and rejection necessitated by Applicant's amendment:

OBJECTION TO THE CLAIMS

3. Claim 6 and claim dependent thereof (claim 7) are objected in depending in canceled claim 5. It is believed to be typographical error. Appropriate correction is required.

CLAIMS REJECTION-35 U.S.C. 112, 1st PARAGRAPH

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no description in the instant specification for the claimed method of **protecting** corneal cells against bacterial invasion by administering into the eye of a subject a pharmaceutical composition comprising a therapeutically effective amount of surfactant protein-D as claimed in claim 24. The instant specification does not enable a method for **protecting** corneal cells against bacterial invasion by administering the compound claimed because there are no working example(s) or data or evidence, except for the mere recitation of protocols on pages 19-29 in the instant specification disclosing methods of administering a collectin and/or surfactant proteins to the eye to treat all kinds of ocular diseases in as subject without presenting any data or evidence to substantiate the protocols.

Although, on paragraph 0023, the instant specification defines the term "treating" as any indicia of success in the treatment or amelioration or prevention of an ocular disease, including any objective or subjective parameter such as abatement; remission; diminishing of symptoms or making the disease condition more tolerable to the patient;

showing in the rate of degeneration or decline; or making the final point of degeneration less debilitating. Also, the term "therapeutic effect" is defined as the reduction, elimination, or prevention of the disease, symptoms of the disease, or side effects of the disease in a subject. However, the only *in vivo* experiment conducted is on Example 6 which discloses *in vivo* model of corneal infection to mice, wherein after anesthesia, three linear scratches were allowed to heal and the mice infected with bacteria and 14 days post-bacterial challenge, corneal disease was scored using two different grading system. Although, there is disclosure for *in vivo* experiment as discussed above in Example 6, however, there is no disclosure for the claimed method of **protecting** corneal cells against bacterial invasion by administering into the eye of a subject a pharmaceutical composition comprising a therapeutically effective amount of surfactant protein-D. The specification discloses only the reduction of invasion of corneal cells against bacterial invasion and **not** "**protecting**" corneal cells against bacterial invasion as claimed in claim 24.

Further, Applicant's claims are directed to "**protecting**", and there is no objective factual evidence in the instant specification to show that protection has occurred since no adequate time was given to mimic the protocol administered in the animal models and allow evaluation of active immune response or inhibition. Thus, one cannot administer at the point of infection and claim protecting a subject for the conditions claimed without appropriate testing for the reasons stated above.

Therefore, in view of the above, the scope of "**protecting**" corneal cells against bacterial invasion are not enabled and speculative, and as such, it would include those

preparation/formulation that have not been shown or taught to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention of **protecting** is enabled, since a vast range of steps, processes and ingredients are contemplated and are encompassed as well as wide range of situations of a method for **protecting** corneal cells against bacterial invasion. The results desired appear to be highly dependent on all variables, the relationship of which is not clearly disclosed.

Therefore, without adequate guidance through working example(s), one of ordinary skill in the art would not predict from the protocols recited on pages 19-29 in the instant specification to achieve a method of **protecting** corneal cells against bacterial invasion by administering into the eye of a subject a pharmaceutical composition comprising a therapeutically effective amount of surfactant protein-D as claimed in claim 24. Thus, the instant specification does not enable any person skilled in the art to which it pertains, or which is most nearly connected, to use the invention commensurate in scope with the claim. In the express absence of one or more examples, evidence and sufficient guidance, the skilled artisan would be faced with undue experimentation for practicing the claimed invention.

OBJECTION TO CLAIMS, ALLOWABLE SUBJECT MATTER

5. Claims 2 and 23 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

ACTION IS FINAL, NECESSITATED BY AMENDMENT

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

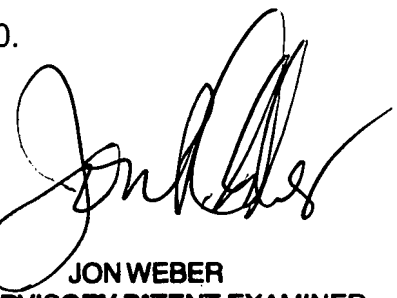
CONCLUSION AND FUTURE CORRESPONDANCE

7. Claims 1, 6-11 and 24 are rejected, claims 2 and 23 are objected and claim 20 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on (571) 272 0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM
May 25, 2007.